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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/767,329	01/29/2004	Sean D. Monahan	Mirus.041.01	6227

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MIRUS CORPORATION
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EXAMINER	
VANIK, DAVID L	

ART UNIT	PAPER NUMBER
1615	

DATE MAILED: 08/04/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/767,329	MONAHAN ET AL.	
	Examiner	Art Unit	
	David L. Vanik	1615	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-24* is/are pending in the application.

4a) Of the above claim(s) *9-20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-8 and 21-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-24* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date 1-10-05
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Receipt is acknowledged of the applicant's Oath or Declaration filed on 4/16/2004. Receipt is also acknowledged on applicant's Information Disclosure Statement filed on 1/10/2005.

Election/Restrictions

1. Restriction to one of the following inventions is required under 35 U.S.C. 121:

   I. Claims 1-8 and 21-24, drawn to a composition comprising a polypeptide-surfactant complex wherein the surfactant is associated with the polypeptide via a **non-covalent bond** and a method of using said composition, classified in class 424, subclass 460.

   II. Claims 9-20, drawn to a composition comprising a polypeptide-surfactant complex wherein the surfactant further comprises a surfactant-chelator and is associated with the polypeptide via a **covalent bond**, classified in class 424, subclass 450.

The inventions are distinct, each from the other because of the following reasons:

2. Inventions I and II are unrelated to one another. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP §

808.01). In the instant case, the methods of Inventions I and II have different modes of operation, functions, and effects. While Invention I is drawn to a composition comprising a polypeptide-surfactant complex wherein the surfactant is associated with the polypeptide via a **non-covalent bond**, Invention II drawn to a composition comprising a polypeptide-surfactant complex wherein the surfactant further comprises a surfactant-chelator and is associated with the polypeptide via a **covalent bond**. Polypeptide/surfactant complexes connected via either a non-covalent or covalent bond differ in scope. As such, the scope of these two inventions is sufficiently distinct to warrant restriction and a reference anticipating one group of inventions would not necessarily render the other inventions obvious.

3. Searching the inventions of Groups I – II together would impose a search burden on the examiner. In the instant case, the search of distinct surfactant/polypeptide complexes imposes a search burden on the examiner.

4. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper.

5. Because these inventions are distinct for the reasons given above and the search required for each subset of Groups I – II are not required for one another, restriction for examination purposes as indicated is proper.

6. Because these inventions are distinct for the reasons given above and have acquired a separate status in the art because of their recognized divergent subject matter, restriction for examination purposes as indicated is proper.

7. Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

8. During a telephone conversation with Mark Johnson on 7/25/2005 a provisional election was made with traverse to prosecute the invention of Group I, claims 1-8, 21-24. Affirmation of this election must be made by applicant in replying to this Office action. Claims 9-20 are withdrawn from further consideration by the examiner, 37 CFR 1.142(b), as being drawn to a non-elected invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 3-8 are rejected under 35 U.S.C. 102(b) as being anticipated by EP 0335133 A2 ('133).

'133 disclose compositions comprising surfactant proteins and phospholipids (abstract). Said protein-based compositions may be attached to a lipid via a non-covalent or covalent bond (page 3, lines 24-27 and page 4, lines 7-18). The compositions contain cell-targeting signals, as they are capable of delivering of the protein/lipid complex to the lungs (page 3, lines 12-13). It is the examiner's position that the surfactant vesicles used to transport proteins to the lungs are liposomes (page 3, lines 24-27).

In terms of the process of preparing said lipid/peptide complex, leuprolide, a nanopeptide, was admixed with lipids (page 5, line 15-25). The solvents were then evaporated (page 5, lines 20-23). It is the examiner's position that, after evaporation of the solvents, the peptide/lipid complex was dried. After the solvent was evaporated from the peptide/lipid complex, a small quantity of ethanol, an aqueous solvent, was added to the complex (page 5, lines 20-23).

The claims are therefore anticipated by EP 0335133 A2 ('133).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the

invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-4, 6-8, 21-22, 24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Zelphati et al (Intracellular Delivery of Proteins with a New Lipid-mediated Delivery System) in view of Maa et al (Biopharmaceutical powders: particle formation and formulation considerations).

Zelphati et al teach protein/lipid complexes capable of delivering a protein to a cell (abstract; page 35104, paragraph 1; page 35107, paragraph 3). By applicant's own admission, a lipid is an example of a surfactant (page 13, lines 28-31). The lipid used in the invention consists of two saturated C-18 alkyl chains and is non-covalently associated with the protein (page 35104, paragraph 1 and page 35108, paragraph 6). The two saturated C-18 alkyl chains are linked to a core lysine residue through 1,3-dipropylamine (page 35104, paragraph 1). The examiner is interpreting the lysine/1,3-dipropylamine liner to be an "interaction modifier" as set forth in the instant claims 3 and 6. In addition, as confirmed by page 16, line 27 – page 17, line 2 of the instant specification, proteins, such as the ones disclosed in Zelphati et al, can be considered

"cell targeting signals." According to Zelphati et al, the protein/lipid complex can be associated or contacted with a cell (page 35107, paragraph 3 and page 35109-35110, paragraph 4).

The process advanced by Zelphati et al for delivering a polypeptide to a cell includes (1) associating a solubilized protein with a lipid, which comprises surfactants, and (2) contacting the protein/lipid complex with a cell (page 35107, paragraph 3 and page 35104, paragraph 1).

Zelphati et al does not teach lyophilizing the protein/surfactant complex.

Maa et al teach the advantages of lyophilizing proteins (abstract). Lyophilizing is a well-known method in the protein art and the advantages of lyophilization are well established. According to Maa et al., protein/peptide related compositions are more stable in the solid state than in the liquid state (abstract). It is advantageous to lyophilize a protein/peptide sample because the solid state is easier to ship/distribute, store at ambient temperatures, and store for long periods of time (abstract). There are other well-known advantages to lyophilizing protein/peptide compositions. For example, lyophilization is a suitable means of increasing protein/peptide concentration and of changing buffers.

Because protein/peptide lyophilization increases storage stability and stability of the protein/peptide at ambient temperatures, one of ordinary skill in the art would have been motivated lyophilize the protein/surfactant complex advanced by Zelphati et al.

Based on the teachings of Maa et al, there is a reasonable expectation that lyophilizing the protein complex set forth by Zelphati et al would increase the storage longevity and stability of the complex at ambient temperatures. As such, it would have been obvious to one of ordinary skill in the art at the time the invention was made to lyophilize the composition advanced by Zelphati et al in view of the teachings of Maa et al.

Claims 1, 3-8, 21-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over US2003/0054007 ('007) in view of Maa et al (Biopharmaceutical powders: particle formation and formulation considerations).

'007 teach compositions and methods of intracellular protein delivery (abstract). The compositions comprise proteins associated with lipids and further encapsulated into liposomes (abstract). According to '007, the protein/lipid association can be ionic (paragraph 0009 and claims 1, 5, 8). In addition, as confirmed by page 16, line 27 – page 17, line 2 of the instant specification, proteins, such as the ones disclosed in '007, can be considered "cell targeting signals." Interaction modifiers, such as glycol-phosphatidylethanolamine, can also be included in the composition (paragraph 0034).

According to '007, the protein/lipid complex can be associated or contacted with a cell (abstract and paragraph 0014). The process for delivering a peptide or protein to a cell comprises: (1) mixing a solution of dried lipid with a protein, (2) forming liposomes, and (3) adding the protein/lipid mixture to cells (paragraph 0036)

'007 does not teach lyophilizing the protein/surfactant complex.

Maa et al teach the advantages of lyophilizing proteins (abstract). Lyophilizing is a well-known method in the protein art and the advantages of lyophilization are well established. According to Maa et al., protein/peptide related compositions are more stable in the solid state than in the liquid state (abstract). It is advantageous to lyophilize a protein/peptide sample because the solid state is easier to ship/distribute, store at ambient temperatures, and store for long periods of time (abstract). There are other well-known advantages to lyophilizing protein/peptide compositions. For example, lyophilization is a suitable means of increasing protein/peptide concentration and of changing buffers.

Because protein/peptide lyophilization increases storage stability and stability of the protein/peptide at ambient temperatures, one of ordinary skill in the art would have been motivated lyophilize the protein/surfactant complex advanced by '007. Based on the teachings of Maa et al, there is a reasonable expectation that lyophilizing the protein complex set forth by '007 would increase the storage longevity and stability of the complex at ambient temperatures. As such, it would have been obvious to one of ordinary skill in the art at the time the invention was made to lyophilize the composition advanced by '007 in view of the teachings of Maa et al.

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. US Patent 5,858,398 is cited as a patent of interest in its disclosure of a non-covalent protein/lipid complex.

Correspondence

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David L. Vanik whose telephone number is (571) 272-3104. The examiner can normally be reached on Monday-Friday 8:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Carlos Azpuru, can be reached at (571) 272-0588. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David Vanik, Ph.D.
Art Unit 1615

8/1/09

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